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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,040	08/16/2005	Herman Jan Coelingh Bennink	0470-050079	6630

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THE WEBB LAW FIRM, P.C.
700 KOPPERS BUILDING
436 SEVENTH AVENUE
PITTSBURGH, PA 15219

EXAMINER	
CHUI, MEI PING	
ART UNIT	**PAPER NUMBER**
1616	

MAIL DATE	DELIVERY MODE
11/23/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,040	COELINGH BENNINK ET AL.	
	Examiner	Art Unit	
	MEI-PING CHUI	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-54,63 and 64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/22/2009 and 10/22/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Action

Receipt of Amendments/Remarks filed on 10/01/2009 is acknowledged. Claims 25-54 and 63-64 are pending in this application. Claims 1-24 and 55-62 have been cancelled; claims 25 and 34-35 have been previously amended; new claims 63-64 are added.

Receipt of two Information Disclosure Statement filed on 10/22/2009 are acknowledged. The Information Disclosure Statements have been considered and placed in the file.

Status of Claims

Accordingly, claims 25-54 and 63-64 are presented for examination on the merits for patentability.

Rejections and/or objections not reiterated from the previous Office Action are hereby withdrawn. The following rejection(s) is/are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

DOUBLE PATENTING

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application

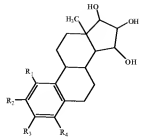
claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 25-32, 45-54 and 63-64 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 20-28, 30 and 33 of co-pending U.S. Patent Application No. 10/532,320.

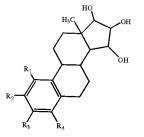
Instant claims are drawn to a method of treating or reducing the risk of developing estrogen-sensitive tumors, i.e. breast cancer, uterine cancer, ovarian cancer, endometriosis or benign prostatic hyperplasia, in a mammal by administering a therapeutically effective amount of an estrogenic component to said mammal, wherein the estrogenic component is represented by the formula as below:



;

in which formula R_1, R_2, R_3, R_4 independently are a hydrogen atom, a hydroxyl group or an alkoxyl group with 1-5 carbon atoms, or precursor capable of liberating a substance or the estrogenic substance as recited therein.

The conflicting claims are drawn to a method of treating or preventing estrogen-suppressed tumors in a mammal by administering to said mammal a therapeutically effective amount of an estrogenic component, wherein the estrogenic component is represented by the formula shown below:



;

in which formula R_1, R_2, R_3, R_4 independently are a hydrogen atom, a hydroxyl group or an alkoxyl group with 1-5 carbon atoms, or precursor capable of liberating a substance or the estrogenic substance as recited therein, wherein the estrogen-suppressed tumors can be benign or malign tumors.

The instant and conflicting claims differ in that the instant claims recite the estrogen-sensitive tumors can be breast cancer, uterine cancer, ovarian cancer, endometriosis, melanoma, and benign prostate hyperplasia, whereas the conflicting claims broadly recite the estrogen-suppressed tumors can be benign and malign tumors.

It would have been obvious for one of ordinary skill in the art to utilize the same estrogenic compound as recited in the conflicting claims in a method of treating or reducing the risk of developing estrogen related tumor as those recited in instant claims because the estrogenic compound is useful for treating estrogen related benign and malign tumors, as suggested by the conflicting claims.

Therefore, one of ordinary skill in the art, at the time the claimed invention was made, would have readily recognized that claims 20-28, 30 and 33 of the co-pending U.S. Patent Application No. 10/532,320 and claims 25-32, 45-54 and 63-64 of the instant application are obvious variant and are not patentability distinct.

The previous provisional rejection, with respect to claims 25-32, 45-54 and 63-64 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 20-28, 30 and 33 of co-pending U.S. Patent Application No. 10/532,320, is maintained.

Response to Arguments

Applicants' arguments filed on 10/01/2009 have been fully considered but they are not persuasive.

Applicants argue that the rejection is pre-mature because claims in the '320 Application have not been allowed. As such, Applicants are not required to address this provisional rejection at this time, and will address this provisional rejection if and when claims 20-24 in the '320 are allowed. Furthermore, the '320 Application has an October 23, 2002 priority date, whereas the instant

application has a July 12, 2002 priority date. A non-statutory obviousness-type double patenting

rejection is not applicable to an application with an earlier filing date because a terminal disclaimer in the instant application would not disclaim any of the patent term (see Remarks: page 7).

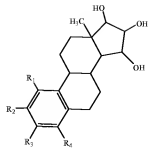
Applicants are reminded that the "provisional" double patenting rejection should continue to be made by the Examiner in each application as long as there are conflicting claims in more than one application unless that "provisional" double patenting rejection is the only rejection remaining in one of the applications." In the instant case, the doubling patenting rejection stated above is not the only rejection remaining in the present application. See MPEP 822.01.

NEW GROUNDS OF CLAIM REJECTION

DOUBLE PATENTING

Claims 25-54 and 63-64 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 13-19 and 21-24 of co-pending U.S. Patent Application No. 10/557,549.

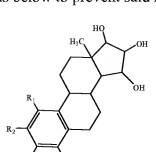
Instant claims are drawn to a method of treating or reducing the risk of developing estrogen-sensitive tumors, i.e. breast cancer, uterine cancer, ovarian cancer, endometriosis, melanoma or benign prostatic hyperplasia, in a mammal by administering a therapeutically effective amount of an estrogenic component to said mammal, wherein the estrogenic component is represented by the formula as below:



;

in which formula R_1, R_2, R_3, R_4 independently are a hydrogen atom, a hydroxyl group or an alkoxyl group with 1-5 carbon atoms, or precursor capable of liberating a substance or the estrogenic substance as recited therein. The instant claims also recite the limitations: (i) the method comprises the uninterrupted administration of the estrogenic component during a period of at least 30 days; (ii) the estrogenic component is administered in an amount of at least 1 µg per kg of bodyweight per day; (iii) the method further comprises co-administration of an aromatase inhibitor in an effective amount to suppress blood serum 17ß-estradiol level to below 10 pg/ml; and (iv) the method comprises oral, transdermal, intravenous, subcutaneous administration of the estrogenic component.

The conflicting claims are drawn to a method of treating musculoskeletal pain in a mammal receiving administration of an estrogen suppressant, i.e. aromatase inhibitor, wherein the method comprises the administration of an effective amount of estrogenic component as represented by the formulas as below to prevent said musculoskeletal pain:



;

in which formula R_1, R_2, R_3, R_4 independently are hydrogen atom, hydroxyl group or alkoxyl group with 1-5 carbon atoms; or precursor capable of liberating the estrogenic compound recited therein. The conflicting claims also recite the limitations: (i) the mammal is suffering from breast cancer, uterine cancer, ovarian cancer, endometriosis, uterine fibroids, melanoma or benign prostatic hyperplasia; (ii) the method comprises the uninterrupted administration of the estrogenic component during a period of at least 5 days; (iii) the estrogenic component is administered in an amount of at least 1 µg per kg of bodyweight per day; (iv) the method further comprises co-administration of an aromatase inhibitor in an effective amount to suppress blood serum 17ß-estradiol level to below 10 pg/ml; and (v) the method comprises oral, transdermal, intravenous, subcutaneous administration of the estrogenic component.

The instant and conflicting claims differ in that the instant claims recite the uninterrupted administration of the estrogenic component during a period of at least 30 days, where the conflicting claims recite the uninterrupted administration of the estrogenic component during a period of at least 5 days. However, it should be noted that the recitation of "the uninterrupted administration of the estrogenic component is for a period of at least 30 days", as claimed is embraced by the conflicting claims, which they recite "the uninterrupted administration of the estrogenic component is for a period of at least 5 days".

Therefore, one of ordinary skill in the art, at the time the claimed invention was made, would have readily recognized that claims 13-19 and 21-24 of the co-pending U.S. Patent Application No. 10/557,549 and claims 25-54 and 63-64 of the instant application are obvious variant and are not patentability distinct.

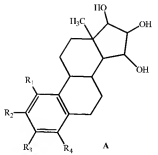
Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

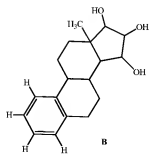
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 28, 38 and 48 are rejected 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite the limitation "the estrogen component according to the method of claim 25 (or claim 35, or claim 45), wherein at least 3 of the groups R_1, R_2, R_3, R_4 represent hydrogen atoms", in which the recitation of the term "at least" is indefinite. According to the structure of the estrogenic component (as represented below), the structures having 3 of the R_1, R_2, R_3, R_4 groups are hydrogen are known. However, the structure having all 4 substituents R_1, R_2, R_3, R_4 groups as being hydrogen atoms cannot be found (see structure B below).



A



B

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Enablement of the Invention

Claims 25-54 and 63-64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 25-54 and 63-64 while being enabling for "treating or reducing the risk of developing estrogen-sensitive tumors: breast cancer, uterine cancer, ovarian cancer, endometriosis, the claims do not reasonably provide enablement for "treating or reducing the risk of developing estrogen-sensitive tumors: melanoma or benign prostatic hyperplasia". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

An analysis of whether the scope of a particular claim(s) is actually supported by the disclosure in a patent application requires a determination of whether the disclosure, at the time of filing, contained sufficient information regarding the subject matter of the claim at issue so as to enable one skilled in the pertained art to use the claimed invention without undue experimentation. *In re Wands*, 8 USPQ 2d 140 (Fed. Cir. 1988). Therefore, the test of enablement is not whether experimentation is necessary, but rather, if experimentation is in fact

necessary, whether it is reasonably considered to be undue. *In re Angstadt*, 190 USPQ 214, 219 (CCPA 1976). Determining the issue of enablement with respect to a claim is a question of law based on underlying factual findings. *In re Vaeck*, 20 USPQ 2d, 1444 (Fed. Cir. 1991). More particularly, there are many factors to be considered in determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph, and whether any necessary experimentation is reasonably considered to be "undue". See *In re Wands* at page 1404. MPEP § 2164.01(a). The court in *In re Wands* set forth the following factors to be considered, which included, without limitation, the: 1). scope or breadth of the claims; 2). nature of the invention; 3). relative level of skill possessed by one of ordinary skill in the art; 4). state of, or the amount of knowledge in, the prior art; 5). level or degree of predictability, or a lack thereof, in the art; 6). amount of guidance or direction provided by the inventor; 7). presence or absence of working examples; and 8). quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

Scope or breadth of the claims:

The claims are broader in scope than the enabling disclosure. The specification merely discloses, without more, the method of treating or reducing the risk of developing estrogen-sensitive tumors: melanoma and benign prostatic hyperplasia by administering the estrogenic compound as claimed with an aromatase inhibitor to a mammal. However, Applicants are purporting that co-administering the estrogenic compound with an aromatase inhibitor in said

method can effectively treat or reducing the risk of tumors, namely melanoma and benign prostatic hyperplasia, in a mammal, even though the multitude of these tumors melanoma and benign prostatic hyperplasia are diversely originated.

Nature of the invention:

The nature of the invention is directed to a method of treating or reducing the risk of developing estrogen-sensitive tumors in a mammal, such as breast cancer, uterine cancer, endometriosis, melanoma or benign prostatic hyperplasia by administering an effective amount of the estrogenic compound and an aromatase inhibitor to a mammal.

State of, or the amount of knowledge in, the prior art:

The currently approach for the treatment of benign prostatic hyperplasia is known, which includes lifestyles changes, medications (e.g. alpha-blockers, 5-alpha reductase inhibitors or anticholinergics), minimal invasive therapies and prostatectomy, and the choice of treatment depends on the prostate's size and overall health of the patient (see Mayo Clinic: Benign Prostatic Hyperplasia).

It is also known in the current state of the art that melanoma arises from many different aspects and causes, such as environment or genetics, for examples. Melanoma can occur in various forms, including ocular melanoma and familial melanoma, and the options for treating melanoma depend on the conditions and the stage of the melanoma, i.e. surgery, radiation therapy, chemotherapy and laser therapy are the common treatments currently available for treating melanoma (see Mayo Clinic: Melanoma Treatments 1-3).

However, the current state of the art does not recognize that estrogenic compounds can be used to effectively treat melanoma and benign prostatic hyperplasia.

Amount of guidance or direction provided by the inventor, presence or absence of working examples:

Although the specification provides some scientific data and working embodiments for the treatment of mammary tumors; however, in the specification there is no working example or guidance provided for the treatment of benign prostatic hyperplasia and melanoma, especially when these two tumors are not occurred at female mammary glands, i.e. breast and uterus.

Quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure:

One of ordinary skill in the art would be required to conduct an undue amount of experimentation to reasonably and accurately determine whether the estrogenic compound when co-administering with an aromatase inhibitor in corresponding instant method does in fact effectively treating benign prostatic hyperplasia and melanoma. Therefore, in conclusion, it is readily apparent from the aforementioned disclosure, in conjunction with a corresponding lack of scientific data and working embodiments, the treatment for, or reduce the risk of developing, benign prostatic hyperplasia and melanoma is not enabled because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Conclusion

Claims 25-54 and 63-64 contain subject matters that may are allowable. However, claims 25-54 and 63-64 are not currently allowed.

Contact Information

Any inquiry concerning this communication from the Examiner should direct to Helen Mei-Ping Chui whose telephone number is 571-272-9078. The examiner can normally be reached on Monday-Thursday (7:30 am – 5:00 pm). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where the application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either PRIVATE PAIR or PUBLIC PAIR. Status information for unpublished applications is available through PRIVATE PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the PRIVATE PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/H.C./

Examiner, Art Unit 1616

/Johann R. Richter/

Supervisory Patent Examiner, Art Unit 1616